REMARKS

This reply is being filed with a Request for Continued Examination (RCE). Upon entry of the present amendments, claims 54-60, 81-85, 88, 94, 96, 100, 107, and 111-122 will be pending. Applicants have amended claims 54, 94, 100, and 107, and added new claims 111-122. Claims 1-53, 61-80, 86, 87, 89-93, 95, 97-99, 101-106, and 108-110 have been canceled. The amendments to claims 54 is supported throughout the specification, e.g., at page 6, line 27 to page 7, line 2; and Examples 9 to 13. Claims 94, 100, and 107 have been amended to depend from claims that have not been canceled. Support for new claims 111-122 can be found throughout the specification, for example, at page 2, line 29, to page 3, line 9; page 5, line 22; page 33, lines 24-25; Examples 8 to 13; and in original claims 15, 17, 41, 46. No new matter has been introduced.

Information Disclosure Statement

On July 11, 2006, applicants filed an information disclosure statement with five pages on Form-1449. In the action mailed August 8, 2006, the Examiner returned initialed copies of only three of the pages. In the previous reply to office action, applicants requested that the Examiner consider the references listed on the forms (listing 19 references, beginning with Alonso et al.) and return an initialed copy. As initialed copies were not enclosed with the Office Action of July 9, 2007, applicants again respectfully request that the Examiner return an initialed copy of the Form-1449. To expedite this process, applicants are enclosing a courtesy copy of the IDS and Form-1449 as filed on July 11, 2006.

Withdrawn Claim Rejection

According to the Office Action at page 2, the Office has withdrawn the rejection of claim 53 as allegedly lacking enablement.

35 U.S.C. § 103

The Office rejected claims 54-60 and 81-110 as allegedly obvious over Barnett et al. (*Vaccine*, 8:869-873, 1997; "Barnett"), Gao et al. (*J. Virol.*, 70(3): 1651-1667, 1996 ("Gao 1"),

Gao et al. (*AIDS Res. Hum. Retrovir.*, 10(11): 1359-1368, 1994; "Gao 2"), and Andre et al. ((*J. Virol.*, 72(2):1497-1503, 1998; "Andre").

According to the Office Action (at page 3):

> Barnett teaches a method of inducing an immune response against HIV in a mammal using a DNA prime and env protein boost immunization method, which is the same vaccination method as the instant invention. Gao teaches a panel of envelope genes from HIV-1 primary isolates of clade A to G, including the env of HIV B715 isolate used in the instant claims. Gao also suggests that the panel of envelope genes from HIV-1 clade A to G prove valuable for AIDS vaccine development efforts targeted at a broader spectrum of viruses. Thus, all the specific vaccination methods, compositions and motivation to combine all these things in order to develop a vaccine regiment [sic] against a broader spectrum of viruses were taught and suggested by the cited references.

The claims, as amended, are directed to a method of inducing immune responses in a mammal by administering a composition that includes (a) at least three and no more than five sets of nucleic acid molecules encoding HIV envelope glycoproteins, such that each of the sets of nucleic acid molecules encodes an envelope glycoprotein of a different primary isolate, and (b) a set of nucleic acid molecules encoding an HIV gag protein. The composition also includes a plurality of sets of isolated HIV envelope glycoprotein molecules of each of the primary isolates in (a). The rejection, should it be applied to the amended claims, is respectfully traversed.

The Office appears to contend that, because Barnett describes using a DNA prime and a protein boost for inducing an immune response against HIV, and that Gao 1 and Gao 2 disclose panels of envelope genes, it would have been obvious to arrive at a method using a polyvalent HIV DNA vaccine and a polyvalent protein boost to induce an immune response against HIV. However, applicants submit that none of the references, individually or combined, suggest using the specific combination and number of DNA and protein vaccines recited in the presently amended claims. Further, the references do not suggest that applicants' claimed method using the recited polyvalent nucleic acid and protein composition (e.g., containing 3 to 5 HIV envelope glycoprotein genes, one HIV gag gene, and 3 to 5 matching envelope glycoproteins) could successfully induce an immune response against a broad spectrum of HIV isolates. Thus, even assuming that skilled practitioners would have been led to combine the teachings of these

references, the instant claims would not have been obvious, as there would have been no reasonable expectation of success.

Barnett describes administering a DNA prime with one gp120 gene and a protein boost with one gp120 protein. It does not provide any information that would have led skilled practitioners to use any combinations of multiple genes and proteins in polyvalent nucleic acid and protein compositions. Thus, it would not have led skill practitioners to applicants' claimed method of using the recited compositions. As Barnett is silent on using polyvalent nucleic acid and protein compositions, the reference does not provide any reasons for skilled practitioners to expect that the recited compositions would work successfully to elicit a broad immune response against a variety of HIV isolates, as further discussed below.

Gao 1 and Gao 2 describe the cloning and analysis of envelope genes from different HIV-1 clades. These references do not disclose methods of administering nucleic acid and protein compositions for eliciting immune responses. The references also do not disclose combinations of genes to be used in such methods. In fact, Gao 1 cautions that "it is impossible to predict which combinations of viral antigens from which subtypes are likely to produce the broadest immunity" (Gao 1, page 1652, right column, lines 2-4). Gao 1 also reports technical challenges in producing constructs capable of expressing envelope genes efficiently. Gao 1 states that efficient expression of the env gene for vaccine applications often requires HIV tat and rev proteins. Isolation of cassettes containing these elements "is possible in principle. However...this approach seems impractical, at least for large numbers of HIV-1 isolates" (Gao 1, page 1662, left column, fourth full paragraph, to page 1663, left column, first paragraph). Thus, not only do Gao 1 and Gao 2 fail to suggest a method using the specific polyvalent compositions recited in the claims, Gao 1 further suggests that it is not at all obvious which combinations of HIV genes would be useful, how many different genes could be included in a polyvalent composition, or whether using a polyvalent composition would even work. Thus, skilled practitioners would not have been led to applicants' claimed method, or expected that the claimed method would successfully induce broad immune responses against HIV.

The present application includes ample data demonstrating that applicants' approach of using specific polyvalent nucleic acid and protein compositions elicits cell mediated immunity and broad antibody responses, including neutralizing responses, against a variety of HIV isolates

of different clades, in various animal models including primates (see, e.g., Examples 8, 9, 12, and 13). That such broad, effective responses could be elicited is not predictable from the cited references. Further, as described in the specification (see, e.g., Examples 8 and 9), a composition containing too many HIV glycoprotein genes (e.g., an 8-valent composition) can actually be less effective than one that contains a smaller number of genes (e.g., a 3-valent composition). Thus, applicants' method of using a composition including, for example, up to 5 envelope glycoprotein genes, can still cover multiple HIV clades to achieve broad antibody responses without compromising the immunogenicity of DNA priming (see page 33, lines 24-27; and Example 13). Reading the cited references, individually or combined, skilled practitioners could not have predicted the impact of any specific number of genes on the effectiveness of DNA priming. Thus, skilled practitioners would not have expected that using the recited compositions could successfully induce broad immune responses against HIV.

Accordingly, the cited references, individually or in combination, do not suggest a method of administering at least three and no more than five sets of nucleic acids encoding HIV envelope glycoproteins from different primary isolates, a set of nucleic acids encoding an HIV gag protein, and a plurality of sets of isolated HIV envelope glycoproteins of each of the primary isolates. Furthermore, skilled practitioners would not have expected that the use of the recited compositions would successfully induce broad immune responses against HIV. Reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicants respectfully request that all claims be allowed. Applicants do not concede any positions of the Examiner that are not discussed above, nor do applicants concede that there are not other good reasons for patentability of the presented claims or other claims. The extension fee and the RCE fee in the amount of $1520 are being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 17738-003001.

Respectfully submitted,

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